American Journal of Hematology 56:224–229 (1997)

# MDS and AML With Trisomy 8 as the Sole Chromosome Aberration Show Different Sex Ratios and Prognostic Profiles: A Study of 115 Published Cases

**Bent Pedersen***

Danish Cancer Society, Department of Cytogenetics, Aarhus C, Denmark

**A number of chromosome aberrations occur nonrandomly as the sole aberration in malignant and premalignant hematological disorders. They imply very different prognoses. For most of them the survival consequences have been established. For trisomy 8, which is the most frequent numerical aberration in myeloid disorders, the prognostic implications have not been investigated. In order to clarify survival in patients with trisomy 8 as the sole aberration, the literature was searched for such cases. In 115 patients survival data were available. In 103 (89.6%), a myeloid disorder had been diagnosed. Acute myeloid leukemia (AML) or a myelodysplastic syndrome (MDS) occurred in 100 cases (87.0%). The median survival was found to be 17.1 months. On multivariate survival analysis (Cox), age above 60 and a leukemic diagnosis were found to be independent adverse prognostic indicators. MDS patients survived significantly longer (median 21 months) than AML patients (median 15 months). In MDS age and in AML the trisomy 8 clonal size was an independent prognostic factor. An unexpected observation was a clear male preponderance in trisomy 8 MDS (about two-thirds of cases). In trisomy 8 AML an approximate 1:1 ratio was found. Browsing of Mitelman's catalog confirmed these ratios. Am. J. Hematol. 56:224–229, 1997.** 

**Key words: chromosome 8; trisomy; prognosis; sex ratio; MDS; AML**

## INTRODUCTION

Trisomy 8 is the most frequent numerical chromosome aberration in acute myeloid leukemia (AML), chronic myeloid leukemia, myelodysplastic syndromes (MDS), and myeloproliferative diseases (MPD), but rare in acute lymphoblastic leukemia (ALL) and other lymphoid disorders [1]. In most cases it develops relatively late in the course of disease, often together with other aberrations. The wide variety of hematological diseases associated with trisomy 8 shows that the aberration is not related to any specific pathogenesis. Rather, it is part of mechanisms driving further progression of malignant and premalignant conditions of the myeloid hemopoietic system.

A number of other chromosome aberrations occur in different hematological diseases and, like trisomy 8, are associated with disease progression. When occurring as sole aberration some of them are prognostically ominous (+13, 7q−, t(1;7)) [2–5] whereas others are compatible with a relatively long survival (5q−, +4) [6–8]. However, the survival of trisomy 8 patients apparently has not been specifically investigated. In order to clarify this the published literature was searched for cases of hematologic disorders with survival data and trisomy 8 as the only chromosome aberration. Trisomy 8 was found to belong to an intermediate group with a median survival longer that those of trisomy 13, 7q−, and t(1;7), but shorter than those of 5q− and trisomy 4. An unexpected finding was that male patients are in massive majority in the trisomy 8 MDS group, whereas in AML the two sexes showed a roughly even distribution.



## MATERIALS AND METHODS

### Patients

The literature was searched for cases with trisomy 8 as the only chromosome aberration and data on survival and

Contract grant sponsor: Danish Cancer Society; Contract grant sponsor: Carl Schepter and Wife's Bequest (the Irma Foundation).

*Correspondence to: Dr. Bent Pedersen, Danish Cancer Society, Department of Cytogenetics, Tage Hansens Gade 2, DK-8000 Aarhus C, Denmark.

Received for publication 16 June 1997; Accepted 9 July 1997

**TABLE I. Distribution on Diagnosis of 115 Patients With Trisomy 8 as Sole Aberration***

| Acute myeloid leukemia[a] | n | Myelodysplasia | n | Others | n |
|---|---|---|---|---|---|
| M1 | 7 | RA | 8 | ALL | 11 |
| M2 | 18 | RAS | 8 | MM | 1 |
| M3 | 2 | RAEB | 17 | PV | 3 |
| M4 | 9 | RAEBt | 4 | | |
| M5 | 7 | CMML | 6 | | |
| M6 | 5 | MDS | 1 | | |
| M7 | 0 | | | | |
| AML | 8 | | | | |
| Total | 56 | | 44 | | 15 |

*M1–M7: AML FAB classes; AML: no FAB class given; RA: refractory anemia; RAEB: RA with excess of blasts; RAEBt: RAEB in leukemic transformation; CMML: chronic myelomonocytic leukemia; MDS: no FAB specification.

**TABLE II. Sex Distribution and Median Survival in Relation to Sex and Diagnosis of 115 Trisomy 8 Cases**

| | Myelodysplasia syndrome | | Leukemias[a] | | Total material[b] | |
|---|---|---|---|---|---|---|
| | n | Median | n | Median | n | Median |
| Men | 32 | 21.0 | 34 | 11.0 | 67 | 15.0 |
| Women | 8 | 20.0 | 38 | 19.5 | 48 | 20.0 |
| P[c] | 0.0001 | 0.573 | 0.168 | 0.044 | 0.031 | 0.125 |

[a]In the group are included 4 cases of RAEBt and one case of myelomaytosis.
[b]Includes 3 cases (two women and one man) with polycythemia vera not included in the myelodyspastic or the leukemic group.
[c]Sex ratios: probability of the observed ratio when the 1:1 ratio is used as null hypothesis (binomial calculation); comparison of survival lengths (log-rank calculation).

diagnosis. Patient sex, age, and the proportion of metaphases containing an extra chromosome 8 were also noted whenever stated [4,9–50]. Information on survival was obtained in 115 cases. Survival was measured from the time of the first observation of trisomy 8. Data on sex and age were obtained in 115 and 107 cases, respectively. The distribution on diagnoses appears in Table I.

### Stratification for Survival Analysis

For survival analysis the material was stratified into a nonleukemic and a leukemic group. The leukemic group included the AML, ALL, RAEBt, and a multiple myeloma case (72 patients in all). The nonleukemic group consisted of 40 MDS and 3 polycythemia vera cases. Further, the material was grouped according to the frequency of trisomy 8 metaphases among those karyotyped (see Table III).

### Statistical Analyses

Univariate (Kaplan-Meier) and multivariate (Cox) survival analyses were carried out for all the available parameters (sex, age, diagnosis, and percentages of trisomy 8 metaphases). For other calculations the various series of quantitative data were analyzed for compatibility with the normal distribution using the Kolmogorov-Smirnov goodness of fit test [51]. As none was compatible or could be transformed into a compatible state, nonparametric methods were used throughout for statistical analysis. For 2 × 2 tables Fisher's exact test was used, and for 2 × n tables the Mann-Whitney test was used. Correlation analyses were carried out with the nonparametric Spearman method [51]. The probabilities of observed distributions on gender were calculated as binomials assuming a true sex ratio of 1:1. All *P* values given in the following are two-sided.

## RESULTS

### Distribution on Gender, Age, and Diagnosis

Among the 115 cases of trisomy 8, AML covered 56 and MDS 44 patients, a total of 100 of the 115 cases (87%). Data on age were available in 107 of the 115 cases. Patient age varied between 1 and 86 years (median: 60). Distribution on diagnosis and sex appears in Tables I and II. The male patients were older than the female patients ($P = 0.003$). Relatively more women had leukemic diagnoses ($P = 0.003$). The MDS group shows a massive male preponderance ($P = 0.0001$), which contrasts to the approximate 1:1 ratio in the leukemic group (Table II). There was no gender-related difference in trisomy 8 clonal size ($P = 0.722$).

### Survival

The overall median survival was 17.1 months (Fig. 1). The female patients tended to survive longer than their male copatients ($P = 0.125$) (Table II and Fig. 2). The difference seems to be due to a significant female survival advantage in the leukemic group ($P = 0.044$). In the MDS group the medians did not differ clearly between the two sexes (Table II).

As appears in Table III, on univariate analysis age was associated with a marginally significant survival difference (medians 20.0 and 10.5 months, respectively) (Fig. 2). Leukemic and nonleukemic cases showed no survival difference in the univariate analysis. If trisomy 8 metaphases covered at least 80% of the mitotic cell population, survival was significantly shorter (median 8.0 months) than seen in cases with smaller clones (median 23 months) (Fig. 2).

The importance of gender, age, diagnosis, and the trisomy 8 clone size was also investigated with a multivariate analysis. Gender seems to be of no prognostic importance, clonal size came out as marginally significant, whereas age and diagnosis were clearly independent prognostic factors (Table III).

As different factors may be of prognostic importance

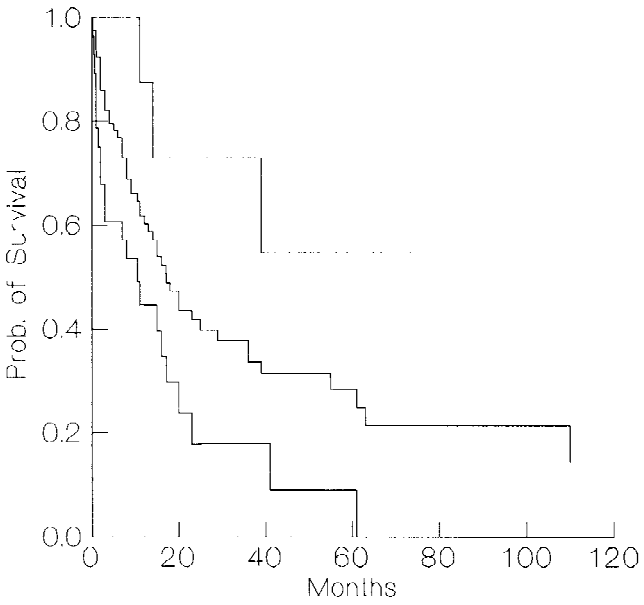


**Fig. 1. The three survival curves represent the total material, those with the most favorable, and those with the poorest prognostic profile, respectively. Median survival of the total material (n = 115) (middle curve) was 17.1 months. Eight patients below 60 years of age and with a nonleukemic diagnosis had the most favorable prognosis and a median survival above 115 months (upper curve). The poorest prognosis (age above 60 and a leukemic diagnosis) was observed in 28 patients and was associated with a median survival of 8 months (lower curve).**

in nonleukemic and leukemic cases, survival was analyzed accordingly after division of the material. Median survival in the nonleukemic and the MDS group was 25 and 21 months, respectively. In the leukemic and the AML group it was 15 and 11 months, respectively. As shown in Table IV, only age was an independent factor in the nonleukemic group. Gender and size of the trisomy 8 clone were without any prognostic relation. In the leukemic group, on the other hand, high trisomy 8 percentages is a clearly adverse prognostic factor. Male gender and age above 60 approached but did not reach statistical significance and so may or may not be independent negative factors.

## DISCUSSION

Occurrence of trisomy 8 as the only chromosome aberration in metaphases of bone marrow or peripheral blood cells is associated with malignant and premalignant conditions of the myeloid hemopoietic system. Out of the 115 cases in the present material, no less than 103 (89.6%) had AML, MDS, or polycythemia vera and only 12 had nonmyeloid diseases. Observation of trisomy 8 in hemopoietic cells consequently implies a high a priori probability that the cells have been aspirated from a patient with a myeloid disease.

### Distribution on Gender

A surprising observation was the marked preponderance of male MDS patients, which contrasted to the near 1:1 ratio in the leukemic group (Table II). In order to test this result in a larger group, Mitelman's catalog [52] was searched for cases with trisomy 8 as the sole aberration. Patient sex and diagnosis were noted. Out of a total of 403 found, 215 were men. Assuming that the true sex ratio is 1:1, the probability of this distribution was 0.032 (binomial calculation), which is in complete agreement with that of the present material (Table II). AML occurred in 208 cases, 108 of whom were men ($P = 0.095$). This probability is in the same order as that found in the present study ($P = 0.168$). MDS occurred in 135 cases, 87 of whom were men (64.4%) ($P = 0.0005$). This result seems to confirm beyond doubt that a marked male preponderance exists in trisomy 8 MDS and an almost equal sex distribution in AML. Male patients tend to outnumber female patients in most malignant diseases. However, in MDS ''males and females are affected almost equally'' [53]. This means that the male preponderance seems to be specific for trisomy 8 MDS.

The MDS trisomy 8 ratio clearly contrasts to that of 5q−, which shows the reverse sex ratio in MDS, although the AML ratio is near 1:1 [6] as found in trisomy 8. In both aberrations women survive longer than men. However, whereas longer female survival in 5q− MDS may explain the female preponderance wholely or partly [6], the situation is the other way round in trisomy 8: the male preponderance manifests itself in spite of shorter male survival and so suggests that the higher male prevalence is due to a higher male incidence.

Conceivably, trisomy 8 cells might proliferate more or survive longer in male than in female patients. The fact that there is no gender-related difference in clonal size ($P = 0.722$) contradicts this explanation, however.

Like trisomy 8, trisomy 13 as the only chromosome aberration shows a marked male preponderance [2]. But here also the phenomenon remains unexplained.

### Factors of Prognostic Importance

The median survival was found to be 17.1 months. This is shorter than that of the 5q− syndrome (61 months) [6], equals that of trisomy 4 (17 months) [54], and exceeds those of trisomy 13 and monosomy 7 (6 months) [2,4] as well as those of 7q− and t(1;7) (11 months) [3,5].

The available data allowed investigation of the prognostic importance of gender, age, diagnosis, and trisomy 8 clonal size. Hematological data were given in too few cases to permit survival analysis. Multivariate survival analysis proved age and diagnosis to be independent prognostic indicators (Table III). Stratification into a nonleukemic and a leukemic group showed that age is an independent prognostic factor in nonleukemic patients,

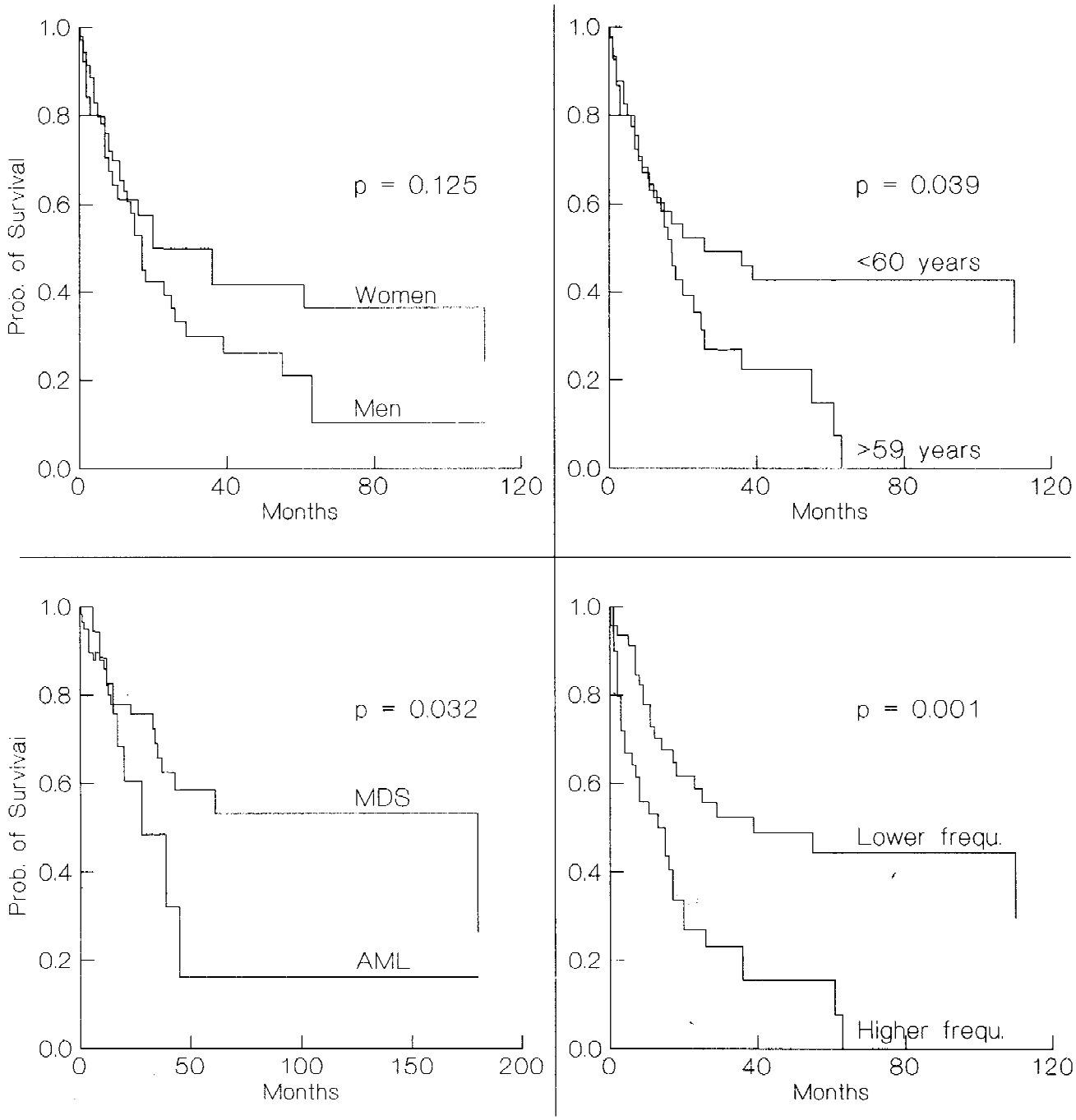


**Fig. 2. Survival: relation to gender, age, diagnosis, and extent of the trisomy 8 clone. Top left: Male vs. female patients; median survival 12.1 and 20.0 months, respectively. The difference is not statistically significant ($P = 0.125$). Top right: Patients below 60 vs. patients above 59 years (median survival 20.0 and 10.5 months, respectively) ($P = 0.039$). Bottom left: MDS vs. AML cases (median survival 21 and 15 months, respectively) ($P = 0.032$). Bottom right: Patients with relatively low frequencies of trisomy 8 metaphases (<80% of those karyotyped) vs. those with high frequencies (⩾80%) (median survival 23.0 and 8.0 months, respectively) ($P = 0.001$).**

whereas gender and trisomy 8 clonal size demonstrated no prognostic importance whatsoever (Table IV). In contrast, in the leukemic group clonal size seems to be the factor of major prognostic importance, whereas gender and age may or may not be prognostically independent.

The different prognostic impact of trisomy 8 clonal size in the two groups is intriguing. The difference is not due to different clonal size ($P = 0.865$). Apparently, clonal expansion is more intimately related to progression mechanisms in leukemic than in nonleukemic pa-

**TABLE III. Survival of Trisomy 8 Patients as a Function of Clinical and Cytogenetic Parameters (*P* Values)**

| | Stratification | Univariate analysis | Multivariate analysis |
|---|---|---|---|
| Gender | Men = 1 (n = 67)<br>Women = 2 (n = 48) | 0.125 | 0.128 |
| Age | <60 = 1 (n = 50)<br>⩾60 = 2 (n = 57) | 0.039 | 0.001 |
| Diagnosis | Nonleukemic = 1 (n = 43)<br>Leukemic = 2 (n = 72) | 0.078 | 0.003 |
| Trisomy 8: % of metaphases | <80% = 1 (n = 50)<br>⩾80% = 2 (n = 43) | 0.001 | 0.059 |

**TABLE IV. Survival of Trisomy 8 Patients With Myelodysplastic and Leukemic Diagnoses (*P* values)**

| | Definition of variables | Univariate analysis | Multivariate analysis |
|---|---|---|---|
| Nonleukemic (43 cases)[a] | | | |
| Gender | M/F | 0.495 | 0.571 |
| Age | <60/⩽60 years | 0.059 | 0.029 |
| +8 metaphases (%) | <80/⩾80 | 0.220 | 0.818 |
| Leukemic (72 cases) | | | |
| Gender | M/F | 0.053 | 0.076 |
| Age | <60/⩾60 years | 0.032 | 0.095 |
| +8 metaphases (%) | <80/⩾80 | 0.001 | 0.0009 |

[a]Forty of the 43 cases had a myelodyspastic syndrome.

tients. Obviously, the same chromosome aberration plays different roles in the processes of MDS and AML progression.

## Conclusion

About 90% of cases with trisomy 8 as the only chromosome aberration have AML or MDS. Among those with MDS about two-thirds are men, whereas the sex ratio is approximately 1:1 in the AML group. To my knowledge, significant deviation from 1:1 in trisomy 8 MDS cases has not been observed earlier. Median survival is 17.1 months. Age above 60, a leukemic diagnosis, and (possibly) presence of trisomy 8 in all or the large majority of karyotyped metaphases were independent adverse prognostic factors, whereas gender seemed without importance. The AML and MDS groups show different median survival and different prognostic patterns. Whereas age is an independent factor in MDS, the trisomy 8 clonal size seems to be the far most important factor in AML. This indicates that trisomy 8 is differently related to the progression mechanisms in the two conditions.

## ACKNOWLEDGMENTS

This work was sponsored by the Danish Cancer Society and aided by grants from Carl Schepler and Wife's Bequest (the Irma Foundation).

## REFERENCES

1. Heim S, Mitelman F: ''Cancer Cytogenetics.'' New York, Alan R. Liss Inc., 1995.
2. Pedersen B, Jensen IM: Trisomy 13: A preferentially male chromosome aberration interfering specifically with myeloid proliferation and differentiation? Cancer Genet Cytogenet 57:79, 1991.
3. Pedersen B, Ellegaard J: A factor encoded by 7q31 suppresses expansion of the 7q− clone and delays cytogenetic progression. Cancer Genet Cytogenet 78:181, 1994.
4. Billström R, Thiede T, Hansen S, Heim S, Kristoffersson U, Mandahl N, Mitelman F: Bone marrow karyotype and prognosis in primary myelodysplastic syndromes. Eur J Hematol 41:341, 1988.
5. Pedersen B: Survival of patients with t(1;7)(p11;p11). Report of two cases and review of the literature. Cancer Genet Cytogenet 60:53, 1992.
6. Pedersen B: Anatomy of the 5q− deletion. Different sex ratios and deleted 5q bands in MDS and AML. Leukemia 10:1883, 1996.
7. Hoyle CF, Bastos Md, Wheatley K, Sherrington D, Fischer PJ, Rees JKH, Gray R, Hayhoe FGH: AML associated with previous cytotoxic therapy, MDS or myeloproliferative disorders: Results from the MRC's 9th AML trial. Br J Haematol 72:45, 1989.
8. Alimena G, Gastaldi R, De Cuia MR, Gallo E, Dallapiccola B: 5q− chromosome in a case of acute nonlymphocytic leukemia (ANLL): The marker of a polyphasic disease? Haematologica 67:261, 1982.
9. Mitelman F, Brandt L, Nilsson PG: Relation among occupational exposure to potential mutagenic/carcinogenic agents, clinical findings, and bone marrow chromosomes in acute nonlymphocytic leukemia. Cancer Genet Cytogenet 6:1229, 1978.
10. Testa JR, Mintz U, Rowley JD, Vardiman JW, Golomb HM: Evolution of karyotypes in acute nonlymphocytic leukemia. Cancer Res 39:3619, 1979.
11. Panani A, Papayannis AG, Sioula E: Chromosome aberrations and prognosis in preleukemia. Scand J Haematol 24:97, 1980.
12. Borgström GH, Teerenhovi L, Vuopio P, Andersson LC, Knuutila S, Elonen E, Chapelle Ad: Chromosome studies in acute lymphoblastic leukaemia (ALL). Scand J Haematol 26:241, 1981.
13. Hagemeijer A, Hählen K, Abels J: Cytogenetic follow-up of patients with nonlymphocytic leukemia. II. Acute nonlymphocytic leukemia. Cancer Genet Cytogenet 3:109, 1981.
14. Mitelman F, Nilsson PG, Brandt L, Alimena G, Gastaldi R, Dallapiccola B: Chromosome pattern, occupation, and clinical features in patients with acute nonlymphocytic leukemia. Cancer Genet Cytogenet 4:197, 1981.
15. Yunis JJ, Bloomfield CD, Ensrud K: All patients with acute nonlymphocytic leukemia may have a chromosomal defect. New Engl J Med 305:135, 1981.
16. Bernstein R, Pinto MR, Morcom G, Macdougall LG, Bezwoda W, Dukes I, Penfold G, Mendelow B: Karyotype analysis in acute nonlymphocytic leukemia (ANLL): Comparison with ethnic group, age, morphology, and survival. Cancer Genet Cytogenet 6:187, 1982.
17. Larson RA, Le Beau MM, Vardiman JW, Testa JR, Golomb HM, Rowley JD: The predictive value of initial cytogenetic studies in 148 adults with acute nonlymphocytic leukemia: A 12-year study (1970–1982). Cancer Genet Cytogenet 10:219, 1983.
18. Li YS, Khalid G, Hayhoe FG: Correlation between chromosomal pattern, cytological subtypes, response to therapy, and survival in acute myeloid leukaemia. Scand J Haematol 30:265, 1983.
19. Bernard P, Reiffers J, Lacombe F, Dachary D, Boisseau R, Broustet A: A stage classification for prognosis in adult acute myelogenous leukaemia based upon patients' age, bone marrow karyotype and clinical features. Scand J Haematol 32:429, 1984.
20. Hörnsten P, Lindquist R, Gahrton G: Prognostic implications of in vitro colony studies and clonal chromsomal aberrations in adults with acute leukaemia. Scand J Haematol 32:297, 1984.
21. Ohyashiki K: Nonrandom cytogenetic changes in human acute leuke-

mia and their clinical implications. Cancer Genet Cytogenet 11:453, 1984.
22. Yunis JJ, Brunning RD, Howe RB, Lobell M: High-resolution chromosomes as an independent prognostic indicator in adult acute nonlymphocytic leukemia. New Engl J Med 311:812, 1984.
23. Goetz P, Stary J, Petrakova A, Hrodek O, Dundekova B, Venclikova K, Zavadova H: Cytogenetic and clinical data of acute lymphoblastic leukemia in children. Clin Genet 24:312, 1985.
24. Testa JR, Misawa S, Oguma N, Sloten Kv, Wiernik PH: Chromosomal alterations in acute leukemia patients studied with improved culture methods. Cancer Res 45:430, 1985.
25. Jacobs RH, Cornbleet MA, Vardiman JW, Larson RA, Le Beau MM, Rowley JD: Prognostic implications of morphology and karyotype in primary myelodysplastic syndromes. Blood 67:1765, 1986.
26. Le Beau MM, Albain KS, Larson RA, Vardiman JW, Davis EM, Blough RR, Golomb HM, Rowley JD: Clinical and cytogenetic correlations in 63 patients with therapy-related myelodysplastic syndromes and acute nonlymphocytic leukemia: Further evidence for characteristic abnormalities of chromosomes no. 5 and 7. J Clin Oncol 4:325, 1986.
27. Misawa S, Hogge DE, Oguma N, Wiernik PH, Testa JR: Detection of clonal karyotypic abnormalities in most patients with acute nonlymphocytic leukemia examined using short-term culture techniques. Cancer Genet Cytogenet 22:239, 1986.
28. Yunis JJ, Rydell RE, Oken MM, Arnesen MA, Mayer MG, Lobell M: Refined chromosome analysis as an independent prognostic indicator in de novo myelodysplastic syndromes. Blood 67:1721, 1986.
29. Pui CH, Raimondi SC, Murphy SB, Ribeiro RC, Kalwinsky DK, Dahl GV, Crist WM, Williams DL: An analysis of leukemic cell chromosomal features in infants. Blood 69:1289, 1987.
30. Rege-Cambrin G, Mecucci C, Tricot G, Louwagie A, Van Hove W, Francart H, Van Den Berghe H: A chromosomal profile of polycythemia vera. Cancer Genet Cytogenet 25:233, 1987.
31. Horiike S, Taniwaki M, Misawa S, Abe T: Chromosome abnormalities and karyotypic evolution in 83 patients with myelodysplastic syndrome and predictive value for prognosis. Cancer 62:1129, 1988.
32. Michael PM, Garson OM, Ekert H, Tauro G, Rennie GC, Pilkington GR: Prospective study of childhood acute lymphocytic leukemia: Hematologic, immunologic, and cytogenetic correlations. Med Pediatr Oncol 16:153, 1988.
33. Misawa S, Yashige H, Horiike S, Taniwaki M, Nishigaki H, Okuda T, Yokota S, Tsuda S, Edagawa J, Imanishi H, Takino T, Inazawa J, Abe T, Nakanishi S, Nakagawa M, Kobayashi H, Maekawa T, Fujii H, Akaogi T, Hayashi H, Fujiyama Y, Kohsaki M: Detection of karyotypic abnormalities in most patients with acute nonlymphocytic leukemia by adding ethidium bromide to short-term cultures. Leuk Res 12:719, 1988.
34. Prigogina EL, Puchkova GP, Mayakova SA: Nonrandom chromosomal abnormalities in acute lymphoblastic leukemia of childhood. Cancer Genet Cytogenet 32:183, 1988.
35. Iurlo A, Mecucci C, Van Orshoven A, Michaux J-L, Boogaerts M, Noens L, Bosly A, Louwagie A, Van Den Berghe H: Cytogenetic and clinical investigations in 76 cases with therapy-related leukemia and myelodysplastic syndrome. Cancer Genet Cytogenet 43:227, 1989.
36. Garipidou V, Yamada T, Prentice HG, Secker Walker LM: Trisomy 8 in acute lymphoblastic leukemia (ALL): A case report and update of the literature. Leukemia 4:717, 1990.
37. Jotterand-Bellomo M, Parlier V, Schmidt PM, Beris P: Cytogenetic analysis of 54 cases of myelodysplastic syndrome. Cancer Genet Cytogenet 46:157, 1990.
38. Kobayashi H, Kaneko Y, Maseki N, Sakurai M: Karyotypically unrelated clones in acute leukemias and myelodysplastic syndromes. Cancer Genet Cytogenet 47:171, 1990.
39. Suciu S, Kruse R, Weh HJ, Hossfeld DK: Results of chromosome studies and their relation to morphology, course, and prognosis in 120 patients with de novo myelodysplastic syndrome. Cancer Genet Cytogenet 44:15, 1990.
40. Iwabuchi A, Ohyashiki K, Ohyashiki JH, Sasao I, Murakami T, Kodama A, Toyama K: Trisomy of chromosome 8 in myelodysplastic syndrome. Significance of the fluctuating trisomy 8 population. Cancer Genet Cytogenet 62:70, 1992.
41. Manso AIG, Marcilla AG, Barreiro E, Gilsanz F: Cytohematologic and cytogenetic prognostic factors at diagnosis and in the evolution of 46 primary myelodysplastic syndromes. Cancer Genet Cytogenet 61:174, 1992.
42. Olufunmilayo I, Olopade MT, Thangavelu M, Larson RA, Mick R, Kowal-Vern A, Schumacher HR, Le Beau MM, Vardiman JW, Rowley JD: Clinical, morphologic, and cytogenetic characteristics of 26 patients with acute erythroblastic leukemia. Blood 80:2873, 1992.
43. Sole F, Prieto F, Badia L, Woessner S, Florensa L, Caballin MR, Coll MD, Besses C, Sans Sabrafen J: Cytogenetic studies in 112 cases of untreated myelodysplastic syndromes. Cancer Genet Cytogenet 64:12, 1992.
44. Dan K, An E, Futaki M, Inokuchi K, Gomi S, Yamada T, Ogata K, Tanabe Y, Ohki I, Shinohara T, Nomura T: Megakaryocyte, erythroid and granulocyte-macrophage colony formation in myelodysplastic syndromes. Acta Haematol 89:113, 1993.
45. Ohyashiki JH, Ohyashiki K, Fujimura T, Kawakubo K, Shimamoto T, Iwabuchi A, Toyama K: Telomere shortening associated with disease evolution patterns in myelodysplastic syndromes. Cancer Res 54:3557, 1994.
46. Parlier V, Vanmelle G, Beris P, Schmidt P, Tobler A, Haller E, Bellomo MJ: Hematologic, clinical, and cytogenetic analysis in 109 patients with primary myelodysplastic syndrome: Prognostic significance of morphology and chromosome findings. Cancer Genet Cytogenet 78:219, 1994.
47. Swansbury GJ, Lawler SD, Alimena G, Arthur D, Berger R, Van Den Berghe H, Bloomfield CD, de la Chappelle A, Dewald G, Garson OM, Hagemeijer A, Mitelman F, Rowley JD, Sakurai M: Long-term survival in acute myelogenous leukemia: A second follow-up of the Fourth International Workshop on Chromosomes in Leukemia. Cancer Genet Cytogenet 73:1, 1994.
48. Tien HF, Wang CH, Chuang SM, Lee FY, Liu MC, Chen YC, Shen MC, Lin KH, Lin DS: Acute leukemic transformation of myelodysplastic syndrome: Immunophenotypic, genotypic, and cytogenetic studies. Leuk Res 19:595, 1995.
49. Mühlematter D, Castagné C, Bruzzese O, Clément F, Schmidt PM, Jotterand-Bellomo M: Tetrasomy 8 in a patent with acute nonlymphocytic leukemia: A metaphase and interphase study with fluorescence in situ hybridization. Cancer Genet Cytogenet 89:44, 1996.
50. Weh HJ, Seeger D, Junge I, Hossfeld DK: Trisomy 8 preceding diagnosis of acute nonlymphocytic leukemia by 2 years in a patient with multiple myeloma without cytological evidence of myelodysplasia. Ann Hematol 72:81, 1996.
51. Sachs L: ''Applied Statistics. A Handbook of Techniques.'' New York: Springer-Verlag, 1978.
52. Mitelman F: ''Catalog of Chromosome Aberrations in Cancer.'' New York: Wiley-Liss, 1994.
53. Beutler E, Lichtman MA, Coller BS, Kipps TJ: ''Williams Hematology.'' New York: McGraw-Hill Inc. 1995, p. 261, 263.
54. Pedersen B: Trisomy 4: Clinical picture, hematology, and survival. Presentation of two cases and review of the literature. Hematol Pathol 6:161, 1992.